

Sex dimorphism in development dynamics and in development progression of morphological features in human fetuses

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The study material comprised 3889 fetuses of both sexes, aged 20–42 weeks. t-Student test has been applied to evaluate the existence of potential sex-dependent differentiation of developmental trends as assessed by weekly measurements of selected somatic features and by the weight of internal organs. The regression coefficients of the analysed variables have been compared against the opposite sex. The rate of development of the analysed features in consecutive weeks has been found to be sex-related. Highest sex-related differences have been observed for the total body weight and for the weight of internal organs, with the exception of the adrenals, and the differences have been significant enough to justify the existence of contrasting, sex-dependent patterns of development of the analysed variables. The development of the analysed morphological features has been depicted by curvilinear regression. When described by various degree polynomials the development course of the analysed features displays sex-related differences. Only the change in the weight of the adrenals is similar for both sexes. The evaluation of the developmental advancement of the analysed features has revealed that they are usually at a more advanced development level in female fetuses.

key words: foetal sex differentiation, rate of feature development, developmental maturity, feature development

INTRODUCTION

This study is part of a larger project focusing on sex dimorphism during foetal development in humans. Sex dimorphism in foetal development has been a subject of numerous studies and controversy [2, 4, 6–9]. The formation of dimorphic differences in somatic features and in the weight of internal organs reported in our earlier study [10] signalled the problem of sex-related differences in foetal development. In order to get a more complete picture of sex-related differences in foetal development other manifestations of sex dimorphism need to be in-

vestigated. As a result, the aim of this study has been to analyse sex-dependent differences in developmental dynamics and in the developmental advancement of somatic features and of the weight of internal organs in humans.

MATERIAL AND METHODS

The study material comprised 3889 fetuses of both sexes (2203 males and 1686 females) aged 20–42 weeks, stillborn in the Obstetrics and Gynaecology Clinic in Poznań in the years 1980–2000. The analysed morphological features (variables) includ-

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ed somatic features (1–7) and the weights of internal organs (8–15). The variables comprised the following items: 1. total body length; 2. crown-rump length; 3. body weight; 4. circumference of the head; 5. circumference of shoulders; 6. circumference of the chest; 7. circumference of the abdomen; 8. brain weight; 9. heart weight; 10. lung weight; 11. liver weight; 12. spleen weight; 13. kidney weight; 14. adrenals weight; 15. thymus weight. None of the stillborn foetuses displayed any signs of developmental pathology and the causes of death have remained unexplained.

T-Student test has been applied to evaluate the existence of potential sex-dependent differentiation in developmental trends and in the rate of development as assessed by weekly measurements of the selected somatic features and the weight of internal organs. Development rate index (DRI) has been used for comparisons of developmental dynamics between the sets of features. The regression analysis ($y = bx + a$) has been used in order to search for the possible existence of sex-related differences in the development of the somatic features. In order to verify the existence of the above differences the “b” directional coefficients of regression for the analysed features have been compared between male and female foetuses by “z” statistics:

$$z = \frac{b_m - b_f}{\sqrt{Eb_m^2 - Eb_f^2}}$$

where: b_m — directional coefficient of linear regression for a given variable in male foetuses; b_f — directional coefficient of linear regression for a given variable in female foetuses; E — standard error for each of the regression coefficients b_m and b_f .

In testing for statistical significance of the difference between regression coefficients, the encountered difficulties are related to not knowing the exact distribution of “z” statistics. It is, however, well known that the value of b/Eb is characterised by central distribution of a t-Student type with N grades of freedom, where $\beta = 0$.

$$\frac{b}{Eb} \approx t_N$$

$N = n - 2 = 23 - 2 = 21$ grades of freedom; β — theoretical directional coefficient of regression.

It may, therefore, be assumed that “z” statistics head asymptotically towards normal distribution if $\beta_m = \beta_f$. As a result, the significance level of a “z” test for $\alpha = 0.05$ does not exactly equal this value and remains its approximation. The accuracy of the significance level has been corrected by construct-

ing the significance ranges for β_m and β_f at the significance level of $1 - \alpha = 0.95$.

$$L = b - t_{\alpha}Eb < \beta < b + t_{\alpha}Eb = R$$

where: t_{α} — value from tables; $t_{\alpha} = t_{N(\alpha)}$; $t_{N(\alpha)}$ — is the upper ?-percentage point of t-Student distribution with N grades of freedom $N = n - 2 = 23 - 2 = 21$.

The subsequent part of the study involved depicting the development of the analysed morphological features by curvilinear regression. The changing developmental dynamics of various features may be documented by expressing the magnitude of a given feature during consecutive weeks of life as a percentage of its final value. Such a procedure, which allowed for the evaluation of developmental progress of the analysed variables in consecutive weeks of intrauterine life, has been adopted in this study with the mean values at week 42 having been assumed as 100%.

RESULTS

The analysis of weekly changes in the analysed variables has revealed that the periods of most intensive accruals of those features, i.e. the periods of most intensive growth of the foetus, are generally the same for both sexes, although it does not mean that the magnitudes of those accruals were the same. The inter-sex analysis of the increases in the analysed variables in a given period of foetal ontogenesis (week 20 – week 42) has therefore been carried out (Fig. 1). The analysis of the curves of the accruals, which depicted the rate of developmental changes, has revealed a different, time-dependent magnitude of the increases in the analysed features in male and female foetuses, i.e. a different rate of the development of the analysed characteristics of both sexes in consecutive weeks of life, yet following a similar change pattern. In some weeks the accruals have been more pronounced in male foetuses, whereas in others in female foetuses. The total increase in the value of each of the analysed features in the period from week 20 to week 42 is significantly more pronounced in male foetuses. The somatic features increase in magnitude almost twice during this period, whereas the increases in the body weight and in the weight of the internal organs are higher and more diversified (Table 1).

Development rate index has been used for comparisons of developmental dynamics between the sets of features (Fig. 2). The DRI values indicate that the rate of development of selected features during the intrauterine period differs and the high rate periods intertwine with low rate ones. Between weeks

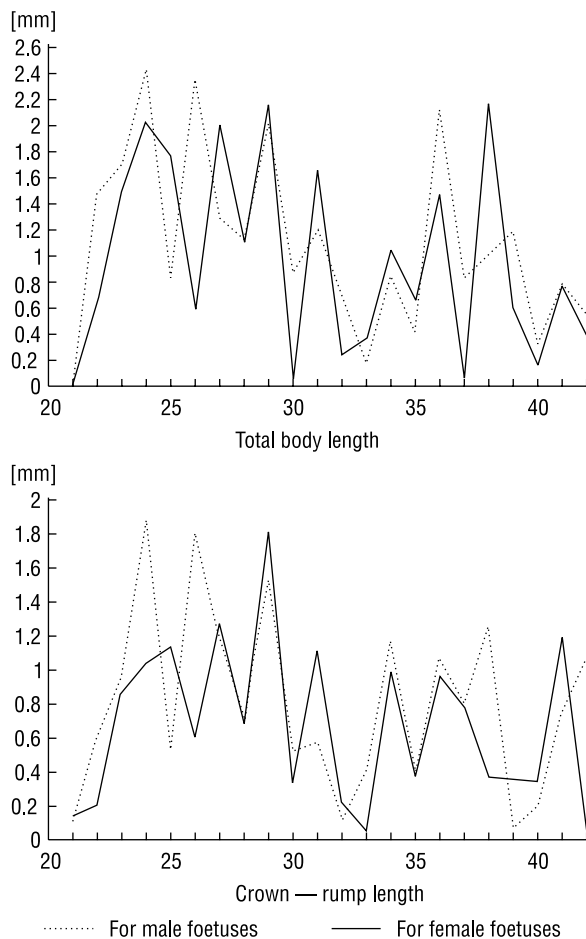


Figure 1. Weekly accruals in the selected features from week 20 to week 42.

21 and 27, between weeks 34 and 36 and during week 42 the values of development rate indices are higher for male foetuses.

Figure 3 displays the development of each of the analysed features in male and female foetuses between week 20 and week 42. With the exception of shoulder, chest and abdomen circumference and the weight of the adrenals the regression coefficients for the analysed features exhibit a significant sex-related differentiation, which indicates the presence of differing, sex-dependent developmental trends for these features. The sex-related differences between directional regression coefficients and the difference significance have been included in Table 2.

The accuracy of the significance level has been corrected by constructing significance ranges for β_m and β_f . Table 3 includes 95% confidence intervals of linear regression directional coefficients for both sexes. If confidence intervals of directional coefficients for a given feature for both sexes are disjointed, then the theoretical values of those coefficients

Table 1. Total accruals and multiplicity of the accruals of the analysed features from week 20 to week 42 of foetal life

Feature	Total of accrual		Multiplicity of the accrual	
	Male foetuses	Female foetuses	Male foetuses	Female foetuses
Total body length	24.47	21.51	1.85	1.74
Crown-rump length	17.71	14.85	1.94	1.77
Body weight	3051.46	2530.68	7.81	6.32
Circumference of the head	15.48	13.10	1.8	1.65
Circumference of shoulders	17.49	16.34	1.92	1.86
Circumference of the chest	15.68	14.06	2.01	1.82
Circumference of the abdomen	16.18	14.36	2.06	1.93
Brain weight	365.34	296.3	6.83	5.78
Heart weight	23.85	19.56	7.31	6.04
Lung weight	28.59	22.71	5.34	4.87
Liver weight	128.16	109.32	5.95	5.36
Spleen weight	11.24	8.9	12.13	9.9
Kidney weight	14.47	11.99	7.16	6.65
Adrenals weight	6.72	6.44	4.34	4.68
Thymus weight	9.38	8.16	8.63	8.92

differ between one another. This method of determining the sex-related differences in regression coefficients allowed us to eliminate those features for which the named difference was close to the critical value of the "z" test (i.e. total body length, crown-rump length and head circumference). Disjointed confidence intervals for simple regression directional coefficients, which at the level of 0.05 confirm the significance of sex-related differences, characterise the body weight and the weights of internal organs with the exception of the adrenals. Significantly higher directional coefficients in male foetuses indicate a higher rate of development of these features in male foetuses.

Rectilinear regression depictions of the analysed features significantly divert from the empirical points and as a result they do not reflect exactly the developmental lines of these features (Fig. 3). The polynomials provide a more precise matching with the empirical points, which is confirmed by the magnitude of the standard error of the estimate, which

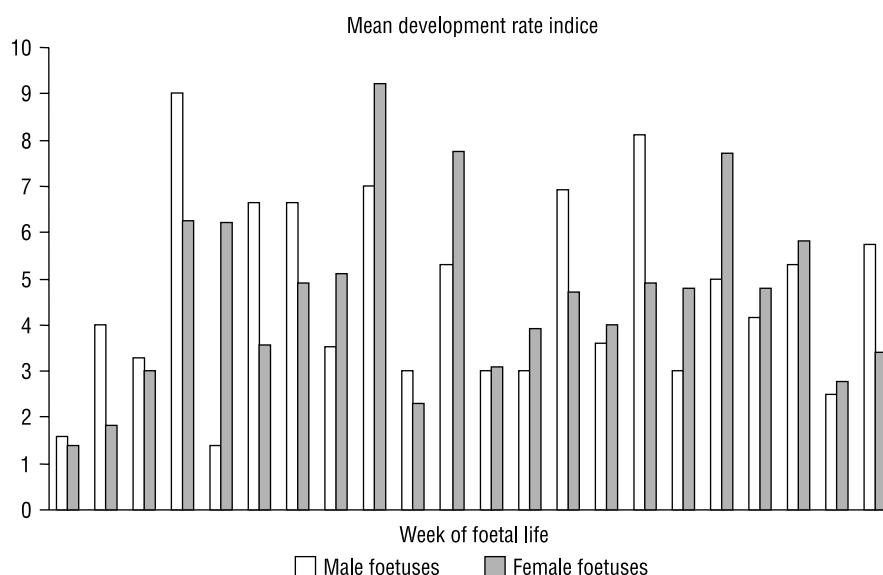


Figure 2. Inter-sex comparison of mean development rate indices of all the analysed features in consecutive weeks (week 21 to week 42).

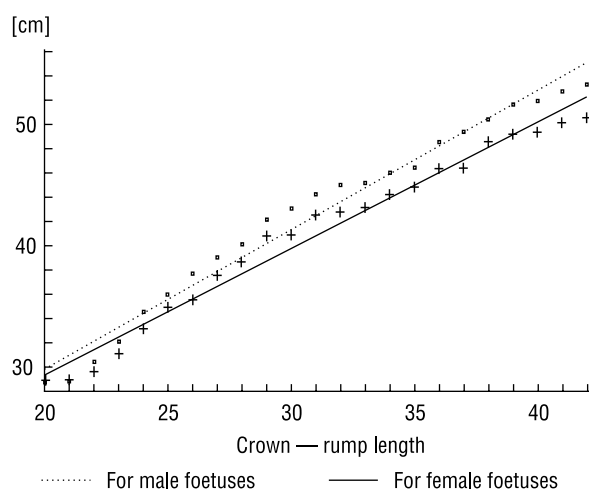


Figure 3. Development of total body length in foetuses of both sexes from week 21 to week 42 as depicted by simple regression model.

reflects the matching of the straight line and the empirical points. The lower the error value the better the matching. The magnitude of the standard error of the estimate for curvilinear regression is significantly lower compared to rectilinear regression representation (Table 4). Therefore, the development of the analysed features has been depicted by curvilinear regression (Fig. 4). The development course of the analysed features, as depicted by various polynomials, differentiates between the sexes of the foetuses, with the most significant differentiation being that of the body weight and the weight of the internal organs, except for the

Table 2. Inter-sex comparison of directional coefficients of linear regression of analysed features

Feature	b_m	Eb_m	b_f	Eb_f	z
Total body length	1.15	0.04	1.04	0.03	2.11*
Crown-rump length	0.82	0.03	0.73	0.02	2.87**
Body weight	141.82	3.44	125.96	3.57	3.20**
Circumference of the head	0.71	0.03	0.63	0.02	2.35*
Circumference of shoulders	0.82	0.03	0.79	0.02	1.02
Circumference of the chest	0.73	0.02	0.70	0.02	1.23
Circumference of the abdomen	0.76	0.02	0.71	0.02	1.36
Brain weight	16.65	0.35	14.38	0.40	4.28**
Heart weight	1.15	0.03	0.96	0.03	4.68**
Lung weight	1.32	0.02	1.11	0.03	5.94**
Liver weight	5.98	0.14	5.13	0.15	4.14**
Spleen weight	0.54	0.02	0.47	0.01	3.39**
Kidney weight	0.67	0.01	0.57	0.01	4.74**
Adrenals weight	0.32	0.01	0.30	0.01	0.52
Thymus weight	0.44	0.01	0.36	0.01	7.12**

adrenals. This observation indicates the existence of developmental parallelism in the compared groups of foetuses.

The developmental progression in foetuses of both sexes, as compared to 42-week-old foetuses, has been

Table 3. 95% confidence intervals of directional coefficients of linear regression of the analysed features for both sexes

Feature	L-R	
	Male fetuses	Female fetuses
Total body length	1.07–1.23	0.97–1.11
Crown-rump length	0.77–0.88	0.68–0.77
Body weight	134.67–148.97	118.54–133.38*
Circumference of the head	0.66–0.77	0.59–0.68
Circumference of shoulders	0.77–0.87	0.74–0.83
Circumference of the chest	0.68–0.79	0.66–0.74
Circumference of the abdomen	0.71–0.80	0.67–0.76
Brain weight	15.93–17.37	13.54–15.21*
Heart weight	1.09–1.21	0.91–1.02*
Lung weight	1.27–1.36	1.05–1.16*
Liver weight	5.68–6.27	4.83–5.43*
Spleen weight	0.51–0.57	0.44–0.50*
Kidney weight	0.64–0.70	0.54–0.60*
Adrenals weight	0.30–0.34	0.27–0.32
Thymus weight	0.43–0.46	0.35–0.38*

Table 4. Standard estimate errors for rectilinear and curvilinear regression

Feature	Male fetuses		Female fetuses	
	Rectilinear regression	Curvilinear regression	Rectilinear regression	Curvilinear regression
Total body length	1.23	0.62	1.08	0.65
Crown-rump length	0.82	0.54	0.68	0.46
Body weight	109.35	46.63	113.53	45.33
Circumference of the head	0.85	0.41	0.72	0.48
Circumference of shoulders	0.82	0.52	0.64	0.54
Circumference of the chest	0.77	0.38	0.60	0.45
Circumference of the abdomen	0.64	0.33	0.74	0.50
Brain weight	11.06	4.86	12.76	6.85
Heart weight	0.93	0.48	0.82	0.44
Lung weight	0.72	0.72	0.86	0.78
Liver weight	4.54	2.44	4.63	2.86
Spleen weight	0.48	0.18	0.47	0.12
Kidney weight	0.45	0.38	0.45	0.34
Adrenals weight	0.26	0.15	0.37	0.17
Thymus weight	0.23	0.21	0.25	0.20

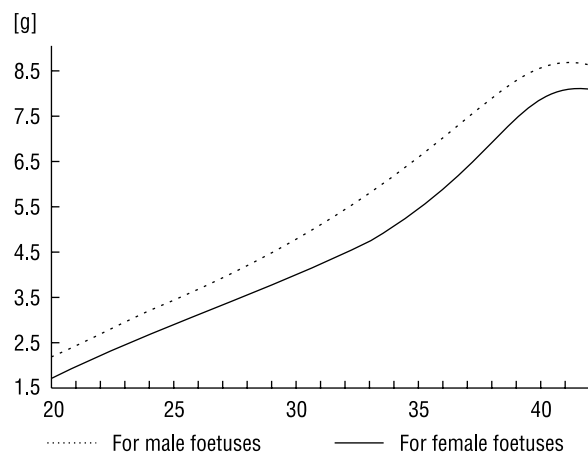


Figure 4. Polynomials which describe the accruals of the adrenals weight in both sexes.

depicted in Figure 5. At week 20 the most advanced of the characteristics include, in order of importance, head circumference, longitudinal features and the remaining circumferences, with body weight and the weight of the internal organs being least advanced. Significant differences in developmental advancement of specific features stem from different developmental dynamics (higher for body weight and the weight

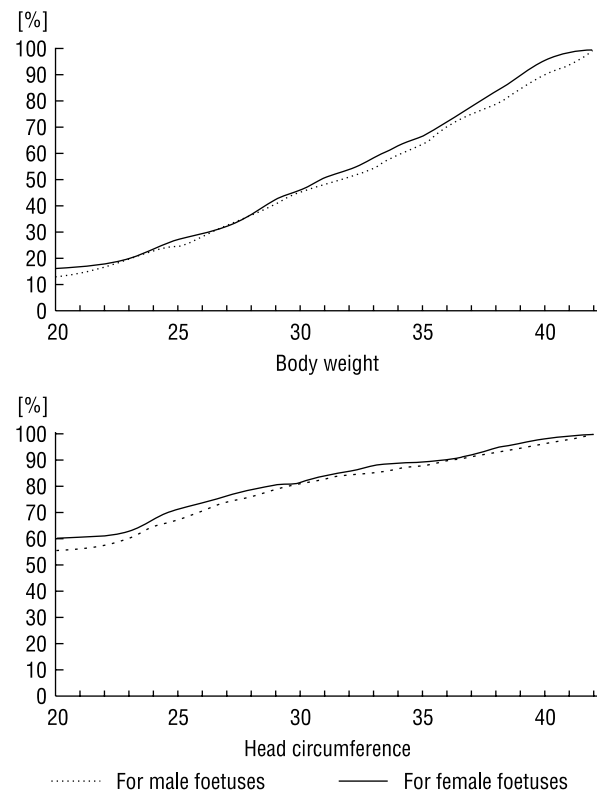


Figure 5. Inter-sex comparison of developmental gradients of selected features.

of internal organs, lower for longitudinal features and the circumferences). The evaluation of the developmental advancement of selected features has revealed that these features are usually either more developmentally advanced in female fetuses or do not exhibit any trend towards higher developmental advancement in any of the sexes.

Because of the high number of the analysed morphological features, the graphic presentations included in this article comprise only some of them.

DISCUSSION

Prenatal sex dimorphism manifests not only through absolute and relative differences between the analysed morphological features but also through differing dynamics of the development of somatic features and sex-dependent weight increase of internal organs. Foetal development is determined by multiple factors and, as a result, the development rate changes with time. It may be assumed that as of the 5th month onwards the development rate begins to decrease [11]. Similar observations have been made by Reicher [7] and Scammon and Calkins [8]. The dynamics of the development of morphological features in the time period analysed in our study has been found to vary. Intertwining periods of accelerated and decelerated growth and development may be distinguished. The periods of most intensive growth are observed generally during the same time in both sexes, yet the rates of growth vary between sexes. The accruals in morphological features may be higher in female fetuses at one time and in male fetuses at another. Such differentiation may be explained by cyclical changes in endocrine metabolism in the pregnant woman, which may differently affect foetal development [3] in male and female fetuses. Similarly, Bożilow et al. [1] have found that the increase in head circumference during foetal development is subject to cyclical, age and sex-dependent changes.

The level of developmental advancement of somatic features confirms the well-known principle of cephalo-caudal development of morphological characteristics in prenatal age. Morphological advancement is highest for (in order of importance) head circumference, total body length and crown-rump length, shoulder, chest and abdomen circumferences, with the least developmental advancement being observed for total body weight. Head circumfer-

ence reaches 90% of its final prenatal value as early as in week 34, whereas body weight reaches 50% of its final value in week 31. A similar degree of developmental advancement has been confirmed by Marecki [5]. As regards the analysed morphological features, female fetuses appear developmentally older than male fetuses, except for the weight of the thymus and the adrenals. Similar results have also been obtained by Malinowski et al. [4].

The cross-sectional nature of the analysed material, which did not allow us to discuss real accruals or decreases in the analysed morphological features, may be considered a limitation of the interpretation capacity of this study (similarly to the majority of other studies on foetal development). Despite great advancement in medical techniques, there is still no possibility of accurate investigation of prenatal development. The ultrasound examination is routinely applied in situations when some foetal or maternal pathology is suspected. As regards the interpretation of such visualisations, it cannot be definitively stated whether these are physiological or pathological representations of foetal development. Moreover, such data are not sufficiently abundant and do not span regular, weekly time intervals. Our cross-sectional research may be, as a result, slightly confounded, yet the error is not significant enough to give up the research while waiting for new research techniques.

CONCLUSIONS

The rate of development of the analysed features in consecutive weeks of foetal life exhibits sex-related differences.

Total accruals for each of the analysed features in the period between week 20 and week 42 are significantly higher for male fetuses, yet the advancement of the analysed features makes the female fetuses developmentally older than the male ones.

Body weight and the weight of internal organs (except for the adrenals) are the features characterised by different, sex-related developmental dynamics. The rate of feature formation is significantly higher in male fetuses.

Accruals in the adrenals weight are similar for male and female fetuses and it is the only one of the investigated features to exhibit developmental parallelism.

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